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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,909	11/04/2003	John R. Erbey II	CV06093	7785

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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
HUYNH, CARLIC K	
ART UNIT	**PAPER NUMBER**
1612	

MAIL DATE	DELIVERY MODE
02/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/700,909	ERBEY ET AL.	
	Examiner	Art Unit	
	CARLIC K. HUYNH	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 11-26* is/are pending in the application.

4a) Of the above claim(s) *24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 11-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *26 October 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks filed on November 27, 2007 is acknowledged.

Status of the Claims

1. Claims 1-3 and 11-26 are pending. Claims 4-10 have been cancelled in a Preliminary Amendment filed on March 21, 2005. Claims 24-26 have been withdrawn in a reply to a restriction requirement filed on November 28, 2006. Accordingly, claims 1-3 and 11-23 are considered herewith.

The rejections under 35 U.S.C. § 112, 1st paragraph have been withdrawn in view of Applicants arguments.

Information Disclosure Statement

The Information Disclosure Statement submitted on October 26, 2007 is acknowledged.

Claim Rejections - 35 USC § 103

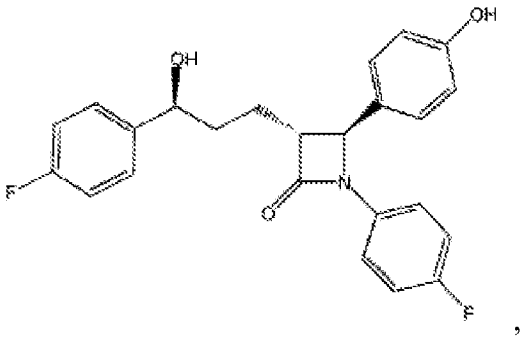
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-3 and 11-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al. (US 2002/0049222) as evidenced by van Heek et al. (British Journal of Pharmacology, 2001, Vol. 134, pp. 409-417) in view of Somers (US 6,147,250).

Yang et al. teach a method for treating conditions associated with inflammation, including rheumatoid arthritis and multiple sclerosis comprising administering modulators of chemokine receptor activity (abstract; and page 9, paragraphs [0357]-[0358]). The pharmaceutical compositions of the present invention include those that contain one or more active ingredients, in addition to a compound of the present invention (page 11, paragraph [0371]). The other active ingredients may be ezetimibe, HMG-CoA reductase inhibitors (e.g. simivastatin and atorvastatin), non-steroidal anti-inflammatory agents, and cyclooxygenase-2 (COX-2) inhibitors (page 11, paragraph [0372]). Yang et al. further teach when using the other active agents, such other drugs may be administered, by a route and in an amount commonly used therefor (page 11, paragraph [0371]).

As evidenced by van Heek, ezetimibe has a chemical structure of,



,

(page 410, figure 1).

Yang et al. do not teach sterol absorption inhibitors that disrupt lipid raft formation of leukocytes.

Somers teaches that HMG-CoA reductase inhibitors lower low density lipoprotein, LDL, levels as well as inhibit the expression of vascular cell adhesion molecule-1, VCAM-1 (column 5, lines 10-14 and column 7, lines 12-14).

Accordingly, absence the showing of unexpected results, it would have been obvious to employ the sterol absorption inhibitor of Yang et al. to disrupt the cell membrane organization of leukocytes and affect adhesion molecule function because the compounds of Somers are HMG-CoA reductase inhibitors and according to Somers, HMG-CoA reductase inhibitors inhibit adhesion molecule function in leukocytes.

The motivation to combine the sterol absorption inhibitors of Yang et al. to the compounds Somers is that the compounds of Somers are HMG-CoA reductase inhibitors and that such HMG-CoA reductase inhibitors inhibit adhesion molecule function in leukocytes.

Regarding the subject has rheumatoid arthritis and other agent as recited in claim 23, it is noted that Yang et al. teach a method of treating inflammatory conditions such as rheumatoid arthritis comprising administering other agents such as cyclooxygenase-2 inhibitors as well as compounds of the present invention (page 11, paragraphs [0371]-[0372]). It would be obvious that the subject has rheumatoid arthritis because the teachings of Yang et al. may also include combinational therapy with cyclooxygenase-2 inhibitors that are used to treat inflammatory conditions.

Response to Arguments

3. Applicant's arguments, see "Remarks" filed on November 27, 2007, with respect to "Rejections under 35 U.S.C. § 103" to claims 1-3 and 11-23 have been fully considered and are not persuasive.

Applicants argue that Yang (US 2002/0049222) teaches a method of treating conditions associated with inflammation such as arthritis and multiple sclerosis, comprising administering modulators of chemokine receptor activity (CCR-2 receptor modulator), whose structure is different from the instant compounds of formulae I-IX. Moreover, Yang teaches co-administration with other ingredients such as ezetimibe and that the co-administration of ezetimibe with the CCR-2 receptor modulator is intended to lower plasma cholesterol rather than to treat an autoimmune disorder.

Applicants further argue Van Heek et al. (British Journal of Pharmacology, 2001, Vol. 134, pp. 409-417) is not directed to the treatment of autoimmune disorders at all but is instead concerned with the effect of ezetimibe in the treatment of artherosclerosis.

Applicants also argue Somers (US 6,147,250) is directed to HMG-CoA reductase inhibitor compounds that are allegedly useful in lowering LDL levels and selectively inhibiting the expression of vascular cell adhesion molecule-1 (VCAM-1). Somers is not directed to, nor does it disclose, the use of sterol absorption inhibitors, such as ezetimibe, or the use of these compounds in the treatment of autoimmune disorders.

Examiner contends Yang et al. teach a method for treating conditions associated with inflammation, including rheumatoid arthritis and multiple sclerosis comprising administering modulators of chemokine receptor activity (abstract; and page 9, paragraphs [0357]-[0358]). The

pharmaceutical compositions of the present invention include those that contain one or more active ingredients, in addition to a compound of the present invention, which includes ezetimibe, HMG-CoA reductase inhibitors (e.g. simivastatin and atorvastatin), non-steroidal anti-inflammatory agents, and cyclooxygenase-2 (COX-2) inhibitors, among others (page 11, paragraphs [0371]-[0372]).

Moreover, Van Heek was used solely to show the structure of ezetimibe (page 410, figure 1) and Somers teaches that HMG-CoA reductase inhibitors lower low density lipoprotein, LDL, levels as well as inhibit the expression of vascular cell adhesion molecule-1, VCAM-1 (column 5, lines 10-14 and column 7, lines 12-14).

Examiner maintains it would have been obvious to employ the sterol absorption inhibitor of Yang et al. to disrupt the cell membrane organization of leukocytes and affect adhesion molecule function because the compounds of Somers are HMG-CoA reductase inhibitors and according to Somers, HMG-CoA reductase inhibitors inhibit adhesion molecule function in leukocytes (e.g. VCAM-1). Accordingly, the motivation to combine the sterol absorption inhibitors of Yang et al. to the compounds Somers is that the compounds of Somers are HMG-CoA reductase inhibitors and that such HMG-CoA reductase inhibitors inhibit adhesion molecule function in leukocytes.

Thus, the Rejections under 35 U.S.C. § 103 to claims 1-3 and 11-23 have been maintained.

Conclusion

4. No claims are allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carlic K. Huynh whose telephone number is 571-272-5574. The examiner can normally be reached on Monday to Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore, Ph.D/
Primary Examiner, Art Unit 1612

ckh